CLINICAL AND ULTRASONOGRAPHIC ASSESSMENT AND ANALYSIS OF LIVER SPAN IN CHILDREN

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CERTIFICATE

This is to certify that **Dr. R. SRI PRIYA,** Post -Graduate Student (June 2006 to March 2008) in the Department of Pediatrics , institute of child health, madras medical college, Chennai- 600 010, has done this dissertation on **"CLINICAL AND ULTRASONOGRAPHIC ASSESSMENT AND ANALYSIS OF LIVER SPAN IN CHILDREN"** under my guidance and supervision in partial fulfillment of the regulations laid down by The Tamilnadu Dr.M.G.R. Medical University, Chennai, for M.D. (Pediatrics), Degree Examination to be held in March 2008.

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CONTENTS

INTRODUCTION

The clinical evaluation of liver size by assessing the liver span is a more reliable index than palpation just below the costal margin[1]. The presence of a generous palpable liver edge does not mean the organ is enlarged. Flattening of diaphragm as a consequence of pneumonia or bronchial air-trapping can push the liver downwards. Sub-diaphragmatic abscess, choledochal cyst, peritoneal cyst or renal mass can be mistaken for enlarged liver.

To accurately determine whether liver is larger than normal, the liver span should be measured. This is best done along the mid-clavicular line, with palpation/ percussion of the lower margin and percussion of the upper margin. This maneuver eliminates erroneous assumptions of hepatic enlargements in these instances in which hyperinflation of the lung results in downward excursion of the sub-diaphragmatic liver.

Hepatomegaly, an enlarged liver is an important clue to a variety of systemic pathological conditions. Alternatively, it may herald the disease of liver itself and palpable liver does not denote hepatomegaly.

In a normal child, liver edge is usually palpable 2cm below right costal margin in mid-clavicular line. In infants liver edge is palpable 2-3cm below right costal margin, while level beyond these parameters indicate hepatomegaly. Liver span is a more reliable indicator.

Hepatomegaly may be a transient finding during systemic viral illness like infectious mononucleosis but persistent hepatomegaly is an indication for further evaluation. A firm enlarged liver may suggest a storage disease, infiltration process or neoplasia. Tenderness of enlarged liver may suggest inflammatory process. Cystic disease of liver may also cause hepatomegaly.

Evaluation of liver size by ultrasound has been found to be both accurate and reliable[2]. However despite widespread clinical use, we know of no generally accepted standards of liver size.

Sonography is routinely used to evaluate visceral organs in children because it offers numerous advantages[3]. There is no radiation. Furthermore the measurement is real time, tri-dimensional and independent of organ function. Sonography can be safely repeated during the examination. However, there are few studies to define the normal limits of organ dimensions in children.

Our purpose is to determine the clinical and ultrasound liver span measurements in various age groups, their correlation and correlation of each with sex, age height and weight.

This study with previous data of normal measurements will be a complete and conventional for reference of pediatric liver size in future.

TOPOGRAPHY

Situated intraperitoneally in the right upper quadrant, the upper surface is convex and nestles the diaphragm typically at the level of fifth or sixth anterior rib in quiet respiration[4]. The lower surface tends to be concave, with gallbladder in it. Although the fundus of the gallbladder may project below and anteriorly to the lower edge, it is not felt in the healthy persons.

The bulk of the liver sits posteriorly, where it cannot be assessed from behind because of intervening retroperitoneal contents, ribs and lumbar musculature. Anteriorly, the liver sits partly above the costal margin, with ribs and lungs supervening and partly below it. The portion extending below or inferior to the costal margin varies and typically runs parallel to the costal margin. However, physicians working in modern imaging departments, like generations of surgeons and anatomists before them, can attest to the degree of variability in the shape of the organ, including the extend to which the lower edge parallels the costal margin and the degree of extension beyond the midline into the left upper quadrant. To some extend, the vertical liver span (the inner distance from the top of the liver dome down to the lower edge) is a function of where in the right hypochondrium the liver edge is palpated or percussed. The falciform ligament joins the mid anterior surface of the liver to the diaphragm and anterior abdominal wall. With respiration, diaphragmatic contraction drives the liver downwards and the anterior surface of the organ slightly rotates to the right. The liver edge moves 1 to3 cm with deep inspiration.

ANATOMY

The liver is the largest organ in the body. There are two anatomical lobes –the right six times the size of the left. In infants the left lobe is larger[5]. Lesser segment of the right lobe is the caudate lobe on the posterior surface and the quadrate lobe on the inferior surface. The lobes are separated anteriorly by a fold of peritoneum called the Falciform ligament and posteriorly by fissure for Ligamentum Venosum and inferiorly by fissure for Ligamentum Teres.

The liver is kept in position by peritoneal ligaments and by the intra abdominal pressure transmitted by the tone of the muscles of the abdominal wall

EMBRYOLOGY AND MORPHOGENESIS

During the early embryonic process of gastrulation, the three embryonic germ layers (endoderm, mesoderm, and ectoderm) are formed. The liver and biliary systems arise from cells of the ventral foregut endoderm[6.] Their development can be divided into three distinct processes. First, through unknown mechanisms, ventral foregut endoderm acquires competence to receive signals arising from the cardiac mesoderm. These mesodermal signals, in the form of various fibroblast growth factors and bone morphogenetic proteins, result in specification of cells that will form the liver and activation of liver-specific genes. This specification occurs in animal models just before visible budding of the liver. These newly specified cells then migrate in a cranial ventral direction into the septum transversum in the 4th wk of gestation to initiate liver morphogenesis. The growth and development of the newly budded liver requires interactions with endothelial cells.

Within the ventral mesentery, proliferation of migrating cells form anastomosing hepatic cords, with the network of primitive liver cells, sinusoids, and septal mesenchyme establishing the basic architectural pattern of the liver lobule The solid cranial portion of the hepatic diverticulum (pars hepatis) eventually forms the hepatic parenchyma and the intrahepatic bile ducts; the caudal portion (pars cystica) becomes the gallbladder, cystic duct, and common bile duct. The hepatic lobules are identifiable in the 6th gestational wk. The bile canalicular structures that include microvilli and junctional complexes are specialized loci of the liver cell membrane; these appear very early in gestation; by 6-7 wk large canaliculi bounded by several hepatocytes are seen. The intrahepatic bile ducts are derived through branching and remodeling of the hepatic duct; formation is complete by the 3rd mo. The cystic duct and the gallbladder are fully recanalized by the 7th-8th wk.

In the hepatic excretory (biliary) system, intercellular bile canaliculi empty into the smallest bile ductules, which unite to form interlobular bile ducts that follow the terminal branches of the portal vein. At the hilum of the liver, the intrahepatic ducts leave the branches of the portal vein and merge to form the extrahepatic biliary system.The ducts of the right and left lobes form the common hepatic duct. The common bile duct is formed from the merger of the common hepatic duct and cystic duct; it extends along the right edge of the lesser omentum, terminating as the intramural papilla of Vater. Union of the biliary tract with the pancreatic ducts forms the ampulla of Vater, which, with the sphincter of Oddi, regulates the flow of bile into the intestine, prevents entry of bile into the pancreatic duct, and inhibits reflux of intestinal contents into the ducts

Fetal hepatic blood flow is derived from the hepatic artery and from the portal and umbilical veins, which form the portal sinus. The portal venous inflow is directed mainly to the right lobe of the liver; umbilical flow is primarily to the left. The ductus venosus shunts blood from the portal and umbilical veins to the hepatic vein, bypassing the sinusoidal network. The ductus venosus becomes obliterated when oral feedings are initiated. The oxygen saturation is lower in portal than in umbilical venous blood; accordingly, the right hepatic lobe has lower oxygenation and greater hematopoietic activity than the left hepatic lobe. The fetal sinusoidal endothelium is the site of large macrophages, which become the Kupffer (reticuloendothelial) cell network.

The transport and metabolic activities of the liver are facilitated by the structural arrangement of liver cell cords, which are formed by rows of hepatocytes, separated by sinusoids that converge toward the tributaries of the hepatic vein (the central vein) located in the center of the lobule. This establishes the pathways and patterns of flow for substances to and from the liver. In addition to arterial input from the systemic circulation, the liver also receives venous input from the gastrointestinal tract via the portal system. The products of the hepatobiliary system are released by two different paths: through the hepatic vein and through the biliary system back into the intestine. Plasma proteins and other plasma components are secreted by the liver. Absorbed and circulating nutrients arrive through the portal vein or the hepatic artery and pass through the sinusoids and past the hepatocytes to the systemic circulation at the central vein. Biliary components are transported via the series of enlarging channels from the bile canaliculi through the bile ductule to the common bile duct.

The liver reaches a peak relative size at the 9th wk at about 10% of the fetal weight. Early in development, the liver is the primary site of hematopoiesis; during the 7th wk, hematopoietic cells outnumber functioning hepatocytes in the hepatic anlage. These early hepatocytes are smaller than at maturity (20 µm vs 30-35 µm) and contain less glycogen. Near term, the hepatocyte mass expands to dominate the organ, as cell size and glycogen content increase. Hematopoiesis is virtually absent by the 2nd postnatal month in full-term infants. As the density of hepatocytes increases with gestational age, the relative volume of the sinusoidal network decreases. The liver constitutes 5% of body weight at birth but only 2% in an adult

ANATOMICAL ABNORMALITIES OF LIVER[5]

- Accessory lobes
- Reidel’s lobe is fairly common and is a downward tongue like

projection of the right lobe of liver.

- Cough furrow on the liver
- Corset liver
- Lobar atrophy
- Agenesis of right lobe.

Mechanisms of Hepatomegaly[6]

INCREASE IN THE NUMBER OR SIZE OF THE CELLS IN THE LIVER

Storage

- Fat: malnutrition, obesity, metabolic liver disease (e.g., diseases of fatty acid oxidation and Reye syndrome-like illnesses), lipid infusion (total parenteral nutrition), cystic fibrosis, diabetes mellitus, medication related, pregnancy
- Specific lipid storage diseases: Gaucher, Niemann-Pick, Wolman disease
- Glycogen: glycogen storage diseases (multiple enzyme defects); total parenteral nutrition; infant of diabetic mother, Beckwith syndrome
- Miscellaneous: α_1-antitrypsin deficiency, Wilson disease, hypervitaminosis A, neonatal iron storage disease
- Viral-acute and chronic
- Bacterial-sepsis, abscess, cholangitis
- Toxic-drugs
- Chronic hepatitis
- Sarcoidosis
- Systemic lupus erythematosus

- Sclerosing cholangitis

INFLAMMATION

- Hepatocyte enlargement (hepatitis)
- Kupffer cell enlargement
- Autoimmune
- Focal nodular hyperplasia
- Nodular regenerative hyperplasia
- Hepatocellular adenoma
- Infantile hemangioendothelioma
- Mesenchymal hamartoma
- Choledochal cyst
- Hepatic cyst
- Hematoma
- Parasitic cyst
- Pyogenic or amebic abscess
- Hepatoblastoma
- Hepatocellular carcinoma
- Angiosarcoma
- Undifferentiated embryonal sarcoma

INFILTRATION

➢ Primary liver tumors

- Secondary or metastatic tumors
- Veno-occlusive disease
- Hepatic vein thrombosis (Budd-Chiari syndrome)
- Hepatic vein web
- Suprahepatic
- Congestive heart failure
- Pericardial disease
- Tamponade
- Constrictive pericarditis
- Hematopoietic: sickle cell anemia, thalassemia

INCREASED SIZE OF VASCULAR SPACE

- Intrahepatic obstruction to hepatic vein outflow

INCREASED SIZE OF BILIARY SPACE

- Congenital hepatic fibrosis
- Caroli disease
- Extrahepatic obstruction

Concepts of normal liver size have been based on age-related clinical indices, such as (1) the degree of extension of the liver edge below the costal margin; (2)

the span of dullness to percussion; or (3) the length of the vertical axis of the liver, as estimated from imaging techniques. In children, the normal liver edge can be felt up to 2 cm below the right costal margin. In a newborn infant, extension of the liver edge more than 3.5 cm below the costal margin in the right midclavicular line suggests hepatic enlargement. Measurement of liver span is carried out by percussing the upper margin of dullness and by palpating the lower edge in the right midclavicular line; it may be more reliable than an extension of the liver edge alone; the two measurements may correlate poorly

The liver span increases linearly with body weight and age in both sexes, ranging from about 4.5-5 cm at 1 wk of age to approximately 7-8 cm in boys and 6-6.5 cm in girls by 12 yr of age[6]. The lower edge of the right lobe of the liver extends downward **(**Riedel lobe**)** and may be palpable as a broad mass in some normal people. An enlarged left lobe of the liver may be palpable in the epigastrium of some patients with cirrhosis. Downward displacement of the liver by the diaphragm or thoracic organs can create an erroneous impression of hepatomegaly

Examination of the liver should note the consistency, contour, tenderness, or the presence of any masses or bruits, as well as assessment of spleen size. Documentation of the presence of ascites and any stigmata of chronic liver disease is important

Ultrasonography is useful in assessment of liver size and consistency.

Hyperechogenic hepatic parenchyma can be seen with metabolic disease (glycogen storage disease) or fatty liver (from obesity, malnutrition, hyperalimentation, corticosteroids).

AIM OF THE STUDY

1. To assess the normal liver span in children of various age groups' clinically and by ultrasound.

2. To correlate the liver span assessed clinically with ultrasound measurements.

3. To correlate the liver span with height, weight, age and sex.

4. To determine the major factor influencing liver span.

JUSTIFICATION

Previously, individual studies to determine clinical liver size and radiological liver size have been done in Indian adult population[7]. But no reference data or study in Indian pediatric population is available. So this prospective study is conducted to determine the clinical and ultrasound liver span measurements in various age groups, their correlation and correlation of each with sex, age, height and weight

REVIEW OF LITERATURE

Lawson et al[8] estimated liver span in infants and children clinically. The liver span in 350 infants and children was determined by percussion of the upper and lower borders in the midclavicular line. Mean liver span was found to be related to age curvilinearly and ranged from a minimum of 1.9 cm at 1 week of age to a maximum of 7.7 cm in males and 6.3 cm in females at 20 years of age. In children with normal growth patterns, age and sex were found to be the major factors influencing liver size. Though height and weight also correlated with liver span, these variables did not add substantially to the correlation using age and sex alone. The presence of minor systemic illnesses, e.g., otitis and gastroenteritis, did not affect liver span. The expected normal values for liver span at different ages for male and female children have been established and provide the basis for comparison during routine physical examination.

Joshi et al[9] compared the accuracy of palpation and percussion in the rural adult population in central India using ultrasound as the reference standards. Inter physician agreement was assessed using the kappa statistics. The kappa values for inter observer agreement between three physicians for the presence of hepatomegaly at palpation (k=0.44-0.53) and percussion (k=0.17-0.33) were low indicating poor reliability of these techniques. They concluded clinical assessment of hepatomegaly by palpation and percussion lacks both accuracy and reliability.

In a study **Skrainka et al**[10], bedside estimation between three groups of physicians was compared to ultrasound and scintiscan. They found bedside estimation of liver span by direct percussion was as accurate as ultrasound, but that indirect estimate of liver span was inaccurate. Scintiscanning during quiet respiration over estimates the liver span in comparison to ultrasound. They concluded that the previous suggestion that clinical estimates of liver span should be abandoned, may be in error.

Konus OL et al[11]evaluated the normal liver Size in children by ultrasonography and the relationships of the dimensions with sex, age, body weight and height. This prospective study involved 307 pediatric subjects (169 girls and 138 boys) with normal physical or sonographic findings who were examined because of problems unrelated to the measured organs. The subjects were 5 days to 16 years old. All measured organs were sonographically normal. Suggested limits of normal dimensions were defined

Longitudinal dimension showed the best correlation with age, body weight, height, and body surface area. Height showed the strongest correlation of all. This correlation was a polynomial correlation

Liver span in normal Indians was studied by **K.Singh et al**[7]. Liver span was correlated to height, weight and age. The liver span showed significant correlation to height, weight and age. Separating sexes did not improve the correlation. The differences in the coefficient of correlation using age or weight, were significantly less than using height ($p<0.002$).the increase in coefficient of correlation in combining age with height was not significant ($p>0.05$). Therefore height was alone the best determinant of liver span. The age, sex and weight had no significant independent correlation

Soyupak SK et al[12] conducted a study to assess the normal liver dimensions in premature and term newborns and determine the acceptable range. A total of 253 (99 preterm and 154 term) healthy newborns were evaluated within the first week of life by sonography. Gestational age ranged from 24 to 41 weeks, weights ranged from 638 to 4800 g. Measurements were compared with gestational age, weight and height of the infants. Normal ranges for kidney, liver and spleen measurements according to gestational age and weight were obtained. They found that weight showed the best correlation with any of the mentioned organ dimensions.

Sapira[13] has noted that the clinical assessment of liver span need not match closely ultrasound or scintigraphic measures, since the clinical worth of a sign is its potential contribution to clinical decision making. The clinical liver span will however will remain the simplest and therefore the most applicable in the developing countries as it is a simple practical measure of liver size

Castell et al[14] estimated the limits of normal liver span in adult Americans and correlated with height and weight. They found that liver span was best predicted by using a combination of height and weight. They also derived tables based on age, sex, height and weight. But the accuracy of their clinical estimates was not confirmed by any reference standards.

Factors affecting liver size in adults are studied by **Wolfgang Kratzer et al**[15] influence of multiple variables on ultrasound liver size was measured by means of co-variance analysis. Results of multi variate analysis showed that the factors body mass index, height, sex and age exerted an influence over liver size. Body mass index and height were most important factors associated with the diameter of the liver measured at the mid-clavicular line. Height was the most important factor influencing longitudinal diameter.

Dittrich M et al[16] studied In 194 healthy children of all ages, sonographic measurements of the liver. It was performed on standardized section planes and normal values established. These measurement values showed an approximately linear increase in the course of development and correlated best with the body length. For a rapid orientational evaluation of the liver size, sonographic nomograms of the individual measurements were developed. On the basis of an index of liver size, which was calculated from the individual measurements, a diagram for simultaneous determination of liver and spleen size could be developed. These nomograms permit objective morphometry of size changes in the two organs.

Haddad-zebouni S et al[17] studied to establish a standard growth curve of hepatic dimension with respect to age, and to find if any relationship existed between hepatic splenic and renal growth curves. One hundred and fifty abdominal ultrasound studies were obtained on 62 male and 88 female normal children free of any chronic disease, whose ages ranged from 0 to 15 years. Hepatic, splenic and renal dimensions were obtained in a similar and reproducible fashion for all patients. A statistical study of the measurements obtained compared to the age was performed by dividing the subjects into five groups according to age, and after calculating the mean size and variance. Standard growth curves for the liver, kidney and spleen were constructed. Compared to age, splenic size follows the same growth as that of the kidneys, with a constant ratio. The growth pattern of the liver parallel the renal curve with a mean difference of 2.72 cm. He concluded a moderate enlargement of spleen and liver is difficult to evaluate only by clinical examination. Ultrasound may detect it by using the kidney size as a reference.

Friis H Ndhlovu et al[18] studied the ultrasound liver dimensions in children of Zimbabwe. 144 Zimbabwean children between 8 and 16 years of age were studied Based on the liver measurement an index of liver size calculated. Height was employed as the independent variable in all multiple regression models. The organometric data are presented as prediction plots, with observed values and fitted regression line with 95% confidence and prediction intervals. The mean spleen volume was 30% larger for boys than for girls, whereas there was no consistent difference in liver size. No effect of growth Z-scores was seen. The measurements were compared with normal dimensions of livers of German children. For a given height, the mean index of liver size was lower in Zimbabwean than in German children, but inter-observer variation could be a possible explanation for this difference.

In a study by **Niederau et al**[2] normal values and upper limits (95th percentile) of liver, spleen, pancreas, and portal vein size were determined prospectively with ultrasound in healthy subjects. Sex, age, weight, height, and body surface area were determined in each case. Since correlation of longitudinal and transverse organ diameters with physical data was poor (r less than or equal to 0.3), the authors did not consider it necessary to correct the measurements accordingly. However, the liver is oriented longitudinally in slender subjects and transversely in heavy subjects; thus both longitudinal and anteroposterior diameters need to be measured, since the longitudinal diameter alone will give too high or too low a value, respectively.

Weisman LE, et al[19] estimated liver size in the normal neonate clinically. Liver span was determined by a pediatrician and pediatric nurse practitioner, in 100 consecutive normal term neonates at 1 and 3 days of life, using four methods. The most reproducible method in estimating liver size in neonates is either (1) percussion of the upper and lower borders of (2) percussion of the upper border and palpation of the lower border. The clinical estimate of liver size in a healthy term neonate is 5.65 cm, with a 95% confidence limit of 4.25 to 7.00 cm. These values provide a basis for comparison during routine examination.

Gotzberger et al[20] studied a method of Alternative sonographic determination of liver size by intercostal scans. In 241 patients hepatic size was first measured in two conventional sections: midclavicular line (MCL) and anterior axillary line (AAL). Additionally, they measured the organs in midaxillary line craniocaudal (MAL) by determination of the cranio-caudal diameter. In 58 patients additional computed tomography was performed due to special diagnostical reasons so that liver size in MCL could be revealed and compared with ultrasonographical values. The mean value in MCL was 10.7 +/- 2.1 cm measured by ultrasound, 11.4 +/- 3.7 cm measured by computed tomography, 14.0 +/- 1.9 cm in AAL and 14.9 +/- 2.0 cm in MAL. In 5% of the cases the liver could not be measured in the conventional sub costal sections due to obesity or masking by gas, but this was possible in MAL. There conclusion revealed a good correlation of liver size in MCL between ultrasound and computed tomography, as well as in the measurement of AAL and MAL diameters. However, even in cases with difficult sub costal approach, intercostal diameters allow for an accurate determination of hepatic size.

Reiff MI, et al[21] Conducted clinical estimation of liver size in newborn infants**.** Liver size was measured in 100 healthy newborn infants of gestational ages 35 to 44 weeks. A mean liver span of 5.9 +/- 0.8 cm was determined in these infants by measuring the distance between the percussed upper and palpated lower liver borders along the midclavicular line. This value correlated well with measurements derived from percussing both borders (r = .8) and correlated poorly with measurements of liver projection below the costal margin (r = .55). He also concluded the practice of reporting liver projection below the costal margin as a single indicator of liver size should be discouraged.

Jungthirapanich J et al[22] proposed a new reference line for measuring the liver size in healthy newborns. The liver span in 103 healthy newborns was determined by percussion and ultrasonic scanning along the midclavicular line (MCL) and the umbilicus-nipple line (UNL). The liver size (mean +/- SD) measured along the MCL was 4.1 +/- 0.7 cm (range 2.7-5.7 cm) by percussion and 4.0 +/- 0.8 cm (range 1.9-6.2 cm) by ultrasonic scanning. Along the UNL, the liver size determined by percussion was 4.0 +/- 0.7 cm (range 2.8-5.8 cm) and 3.7 +/- 0.8 cm (range 1.4-5.8 cm) by ultrasonic scanning. The correlation coefficient between liver measurement along the MCL and UNL by percussion and ultrasonic scanning was good and statistically significant ($r = 0.95$, $p < 0.0001$ and $r = 0.83$, $p < 0.02$, respectively). The new reference line for measuring the liver size, the UNL, should allow the clinician to determine the liver size more easily and may improve the accuracy in examining the liver.

Carpentieri U, et al[23] studied Liver size in normal infants and children. Liver span of normal infants and children 2 months to 5 years of age was found to be significantly correlated with body height, weight, surface area, and age. However, it was best correlated with body surface area, reflecting a constant relationship between body size and liver size.

Chen CM et al[24] **analyzed** the clinical and ultrasound measurements in Chinese neonates. The liver span measurement by clinical methods with percussion and percussion/ palpation correlated well with ultrasound.

Stephen et al[25] compared techniques of clinical estimation of liver size and analyzed sources of error. They inferred clinical estimation of liver size using radio isotope scintiscan as a standard of reference has been shown to be very inaccurate. The main source of error is in the location of the upper border of the liver. Physical characteristics of the patient influenced this measurement.

Naftalis and Leevy[26] found an excellent correlation between the liver sizes on clinical estimation and scan.

Kasales CJ et al[27] studied the **i**maging variants of the liver, pancreas, and spleen and explored the wide variability in appearance of the normal liver, spleen, and pancreas during cross-sectional imaging (CT, US, and MRI), stressing a thorough understanding of normal anatomy and the affect of physiologic variants.

Naveh and Berant[28] reviewed the literature and compiled norms for clinical liver span for various age groups Newborn -5.5, 2 months -5cm, 1 yr -6cm, 2 yr – 6.5cm, 3 yr -7 cm, 4 yr – 7.5cm, 5 yr – 8cm, 6 yr onwards up to 12 yrs – 9 cm.

Normal standards of liver dimension and relationship with sex, age, weight and height in healthy school going children of age group seven to fifteen years was evaluated by **Safak et a**l[3]. there was no significant difference in organ dimension with respect to sex ($p>0.5$). Weight showed the best correlation of all the parameters.

Sonographic evaluation of liver size in school age children was done by **Sarac et al**[32]. Normal liver size in 350 children of age group seven to twelve years was assessed. The liver span in boys ranged from 11.8 to 12.4cm and 11.3 to 12.1cm in girls. The liver span in boys was more than girls. But there was no statistically significant difference.

MATERIALS AND METHODS

DESIGN

Prospective cross sectional survey

PLACE OF STUDY

This study was conducted in the OPD of Institute of child health and hospital for children, Egmore, Chennai. It included newborn, vaccination clinic, general outpatient departments.

PERIOD OF STUDY

From October 2006 to October 2007.

METHODOLOGY

A. Subject selection

1. Inclusion criteria

a. Newborn – babies attending the wellbaby clinic at maternity hospital newborn OPD.

b. Accompanying siblings of children attending pediatric OPD.

c. Children attending immunization clinic for immunization

d. Children attending OPD with minor dermatological problems like furuncles, hypo pigmented patches, eye problems like squint, refractory error, surgical problems like phimosis, paronychia.

2. Exclusion criteria

a. Children with fever of any cause were excluded.

b. Children with any systemic illness- cardiovascular, respiratory, neurological and abdominal problems and /or significant illness in recent past were excluded.

c. Imaging exclusion criteria were parenchymal mass lesions and cyst.

SAMPLE SIZE

By analyzing previous studies and by using data derived from pilot study, sample size was determined. Total sample size 600. At each age fifty observations were taken (25 male and 25 female). Sampling technique - Stratified random sampling.

METHODOLOGY

The liver span in the mid-clavicular line was determined by a standardized technique. At the time of examination, the children were lying in a supine position and breathing quietly. The pleximeter finger was always perpendicular to mid-clavicular line. Percussion was done starting from the right second inter-costal space in mid-clavicular line. Typical lung field resonance was heard. Gradually moved down, one rib space at a time, percussing until the tone changes because of the inter position of the dome of the liver behind the air filled lung. The upper border was identified usually by a slightly harder percussion. The lower border was determined by soft percussion starting in the right lower abdominal quadrant and ascending towards the liver[5]. We chose to percuss both upper and lower liver borders because young children were unable to continue sustained full inspiration needed for accurate palpation. Nevertheless palpation of the lower liver edge was attempted during quiet breathing on each child. When palpable the edge was most commonly within 0.5cm of the change in percussion note. A pen mark was made on the skin corresponding to the middle of the pleximeter finger. The distance between the pen marks were measured in centimeters. Estimation of liver span was made independently by two observers. Total span was measured to the nearest half centimeter with tape measure.   Weight and height were noted with the use of a infantometer/stadiometer and weighing scale.

Within one hour of physical examination an independent sonographic estimation was made at the same parasaggital locus in supine position.

Sonographic examination was performed with high resolution real time scanner LOGIQ 500MD with 3.5 MHz convex transducer. Transducer is placed transverse and towards right shoulder. The longitudinal axis was measured after clear visualization of liver in mid-clavicular plane. Upper most edge under the dome of the diaphragm was defined as the upper margin whereas the lower most edge was defined as the lower margin and the distance between the two measured in mid-clavicular line[29]. Each child was measured three times and the mean value was recorded as the absolute length. All measured livers had a normal position and echo texture. Informed consent was obtained from parents of all children involved in this study.

STATISTICAL METHODS

The mean clinical liver span, ultrasound liver span and their 95th percentiles of various age groups are tabulated. Inter observer agreement was analyzed using Intraclass correlation coefficient.

Correlation between the clinical and ultrasound liver span measurements were studied using Pearson's correlation.

Correlation of liver span with age was derived from Spearman's correlation. Mean and SD of liver span of both sexes were obtained individually and p value calculated.

Linear regression analysis was done to study the influence of age, sex, weight and height on the liver span. Statistical analysis was done using Spss software.

RESULTS AND ANALYSIS

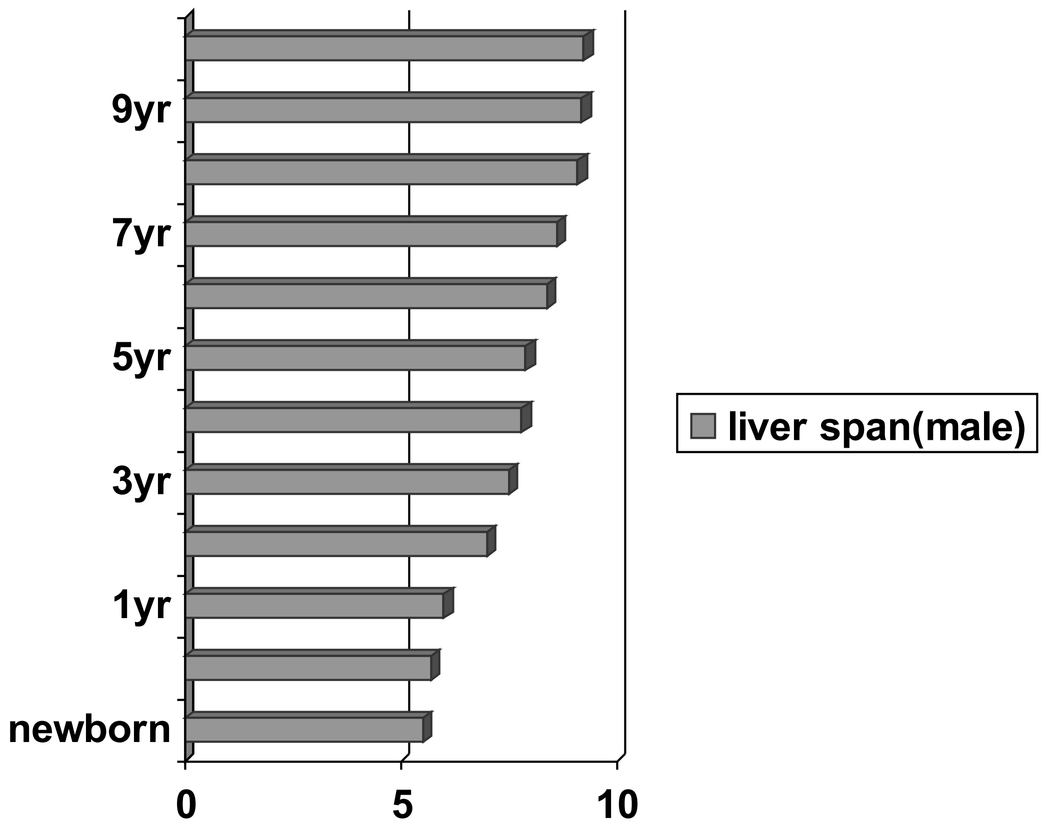
From the data obtained in six hundred patients, mean clinical liver span, age wise and sex wise are tabulated.

CLINICAL LIVER SPAN

AGE	MALE		FEMALE	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
NEWBORN	5.5	0.479	5.7	0.354
INFANCY	5.7	0.52	5.8	0.54
1YR	6.0	0.433	6.2	0.433
2YR	7.0	0.479	6.7	0.456
3YR	7.5	0.500	7.3	0.577
4YR	7.8	0.520	7.6	0.515
5YR	7.9	0.577	7.7	0.433
6YR	8.4	0.599	8.2	0.520
7YR	8.6	0.595	8.5	0.612
8YR	9.1	0.595	9.0	0.736
9YR	9.2	0.520	9.1	0.661
10-12YR	9.25	0.765	9.2	0.677

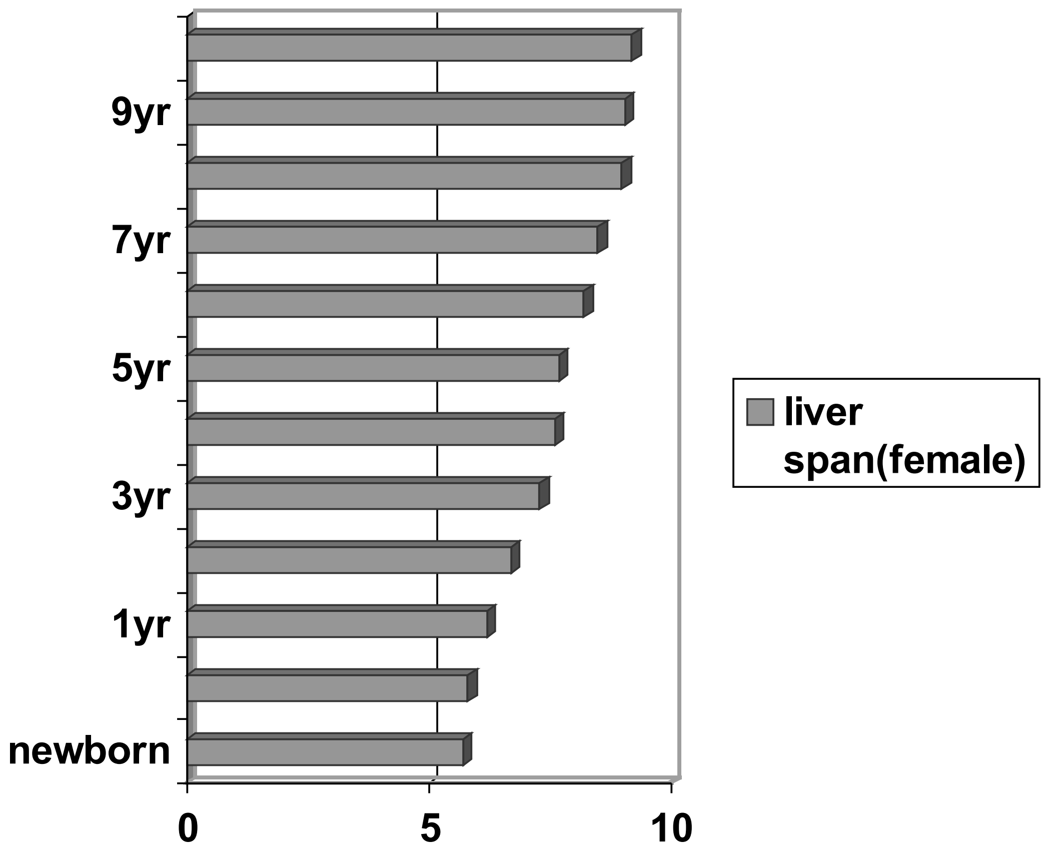
The liver span increases with increasing age. Up to one year the liver span is higher in girls. From two years, it is higher in boys.

CLINICAL LIVER SPAN (MALE)



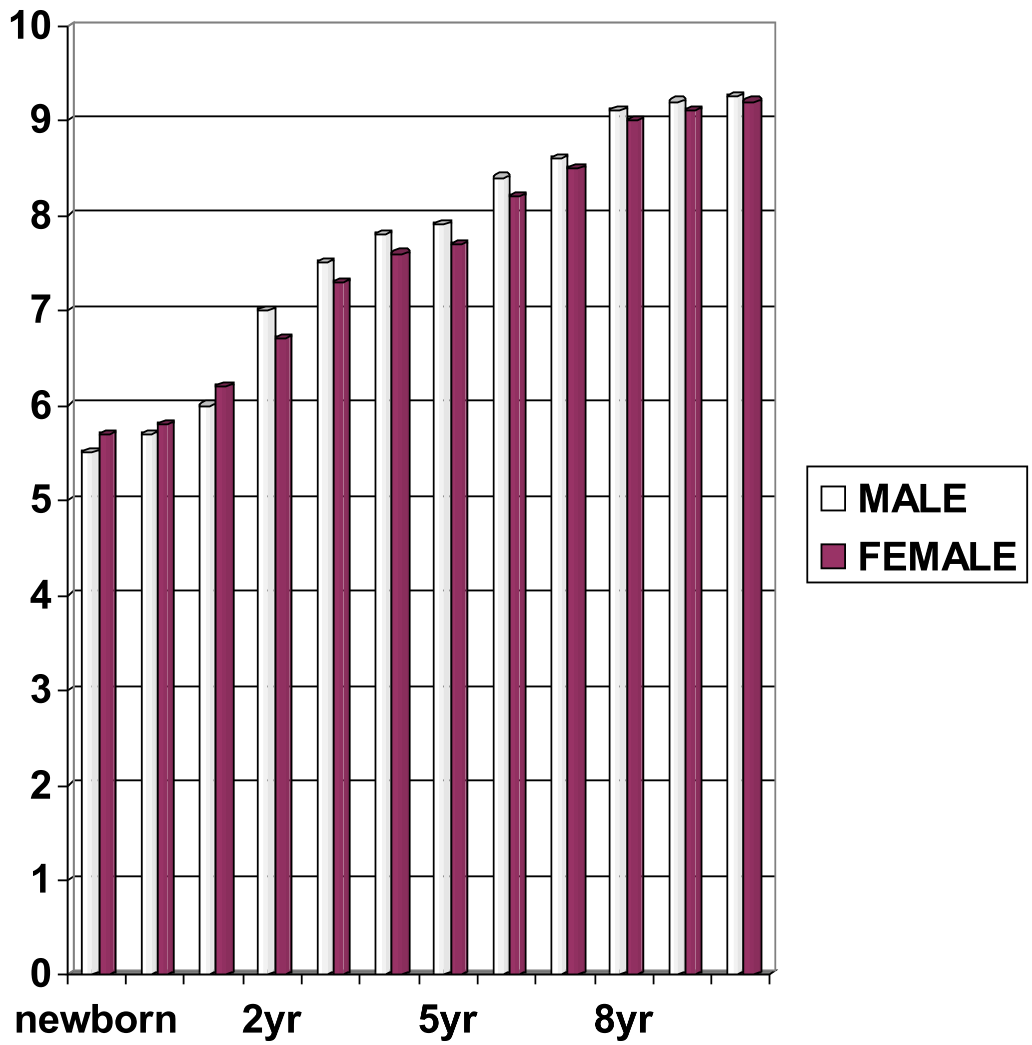
The mean liver span in boys ranges from 5.5 to 9.5cm from newborn period to 12years.

CLINICAL LIVER SPAN (FEMALE)



The mean liver span in girls ranges from 5.7 to 9.2cm from newborn period to 12years.

CLINICAL LIVER SPAN



The above bar diagram shows comparison of clinical liver span in male and female children. The liver span is found to be higher in boys after the age of 2years.

CLINICAL LIVER SPAN

AGE	MALE	FEMALE	MEAN LIVER SPAN	STANDARD DEVIATION	95TH PERCENTILE
NEWBORN	5.5	5.7	5.6	0.429	6
INFANCY	5.7	5.8	5.75	0.527	6.7
1YR	6.0	6.2	6.1	0.440	7
2YR	7.0	6.7	6.85	0.487	7.5
3YR	7.5	7.3	7.4	0.544	8
4YR	7.8	7.6	7.7	0.515	8.5
5YR	7.9	7.7	7.8	0.505	9
6YR	8.4	8.2	8.3	0.535	9.5
7YR	8.6	8.5	8.55	0.600	9.7
8YR	9.1	9.0	9.05	0.753	10.2
9YR	9.2	9.1	9.15	0.625	10.5
10-12YR	9.25	9.2	9.225	0.598	10.7

Clinical liver span- male female, mean liver span and 95th percentile are tabulated.

In the newborn period, the mean liver span for boys is 5.5 cm. For girls of this age group is 5.7cm. In the newborn period, the mean liver span for girls is higher than the boys. Average liver span in newborn period is 5.6cm.

In infancy the mean liver span for boys is 5.7cm. For girls of this age group is 5.8cm. In infancy the mean liver span for girls is higher than the boys. Average liver span clinically in infancy is 5.75cm.

In the one year age group, the mean liver span for boys is 6cm. For girls of this age group is 6.2cm. At one year the mean liver span for girls is higher than the boys. Average liver span clinically in one year age group is 6.1cm.

In the two year age group, the mean liver span for boys is 7cm. For girls of this age group is 6.7cm. At two years the mean liver span for boys is higher than the girls. Average liver span clinically in two year age group is 6.85cm.

In the three year age group, the mean liver span for boys is 7.5cm. For girls of this age group is 7.3cm. At three years the mean liver span for boys is higher than the girls. Average liver span clinically in three year age group is 7.4cm.

In the four year age group, the mean liver span for boys is 7.8cm. For girls of this age group is 7.6cm. At four years the mean liver span for boys is higher than the girls. Average liver span clinically in four year age group is 7.7cm.

In the five year age group, the mean liver span for boys is 7.9cm. For girls of this age group is 7.7cm. At five years the mean liver span for boys is higher than the girls. Average liver span clinically in five year age group is 7.8cm.

In the six year age group, the mean liver span for boys is 8.4cm. For girls of this age group is 8.2cm. At six years the mean liver span for boys is higher than the girls. Average liver span clinically in six year age group is 8.3cm.

In the seven year age group, the mean liver span for boys is 8.6cm. For girls of this age group is 8.5cm. At seven years the mean liver span for boys is higher than the girls. Average liver span clinically in seven year age group is 8.55cm.

In the eight year age group, the mean liver span for boys is 9.1cm. For girls of this age group is 9cm. At eight years the mean liver span for boys is higher than the girls. Average liver span clinically in eight year age group is 9.05cm.

In the nine year age group, the mean liver span for boys is 9.2cm. For girls of this age group is 9.1cm. At nine years the mean liver span for boys is higher than the girls. Average liver span clinically in nine year age group is 9.15cm.

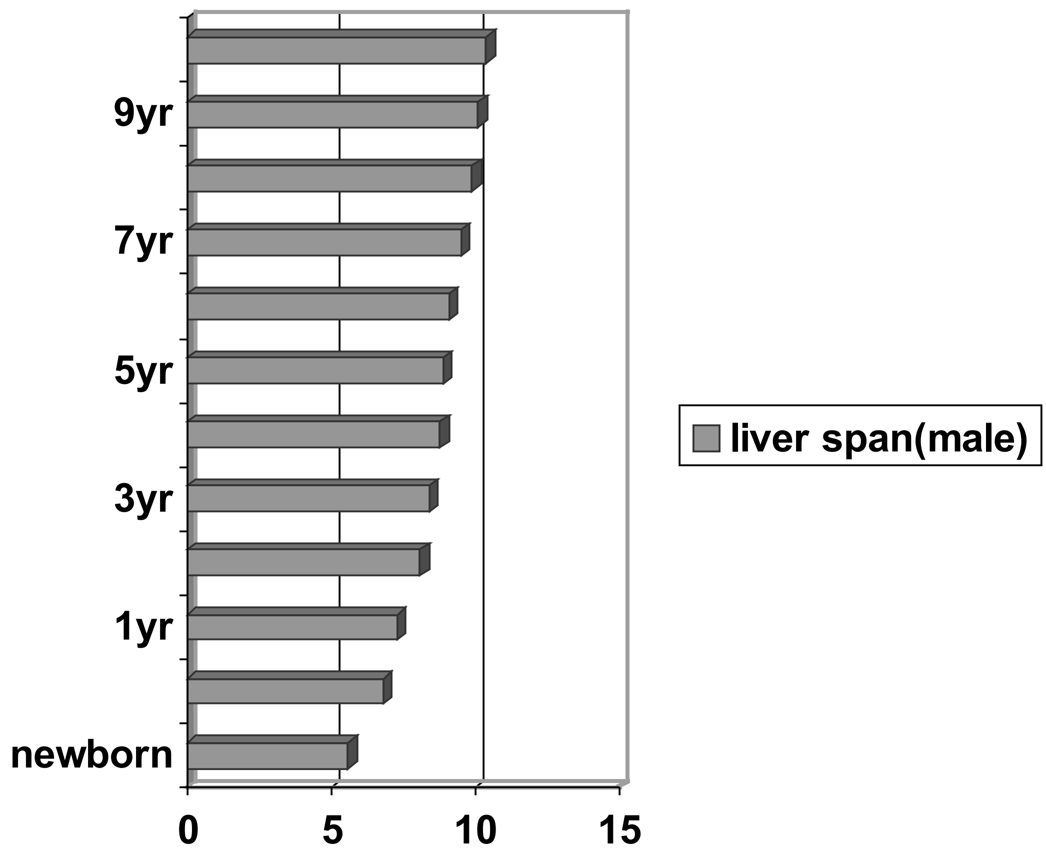
In the ten to twelve year age group, the mean liver span for boys is 9.25cm. For girls of this age group is 9.2cm. At ten to twelve years the mean liver span for boys is higher than the girls. Average liver span clinically in ten to twelve year age group is 9.23cm.

ULTRASOUND LIVER SPAN

From the data obtained, mean ultrasound liver span, age wise and sex wise are tabulated.

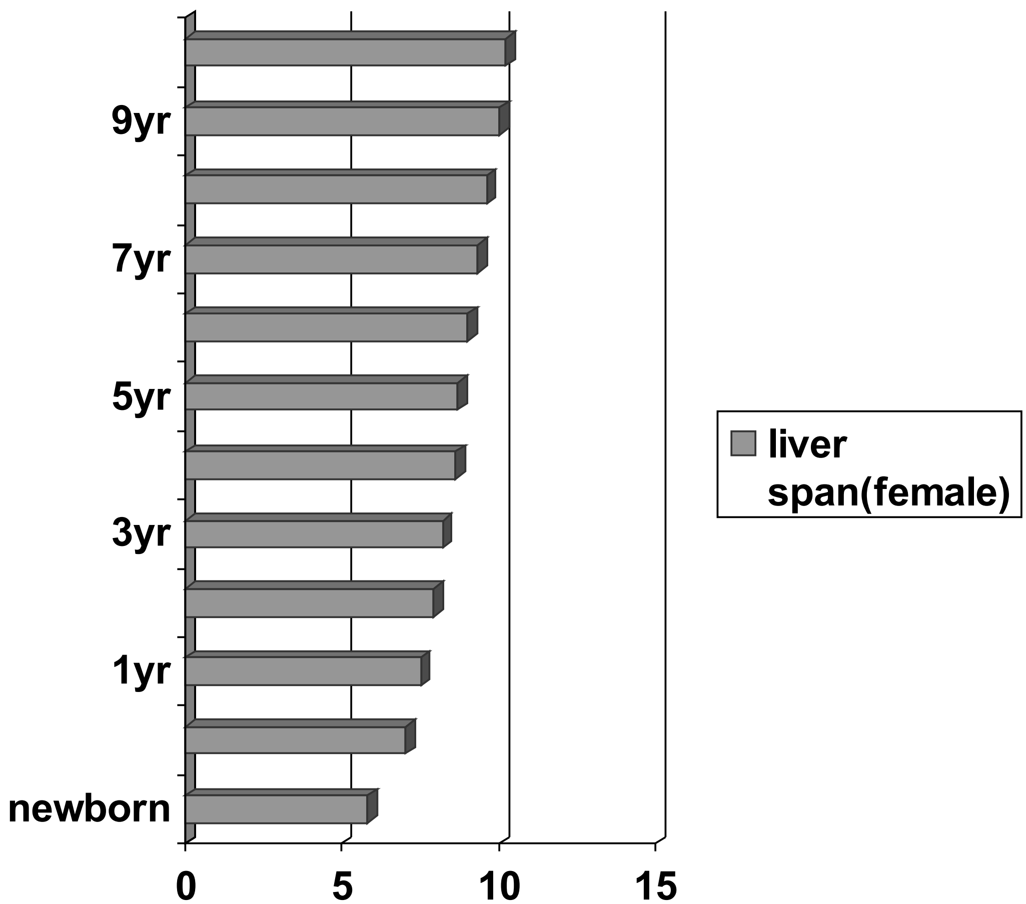
AGE	MALE		FEMALE	
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION
NEWBORN	5.6	0.389	5.8	0.339
INFANCY	6.4	0.713	6.6	0.77
1YR	6.9	0.742	7.3	0.686
2YR	8.1	0.773	7.9	0.657
3YR	8.4	0.334	8.2	0.526
4YR	8.8	0.430	8.6	0.383
5YR	8.9	0.594	8.7	0.483
6YR	9.1	0.539	9.0	0.583
7YR	9.5	0.550	9.3	0.789
8YR	9.9	0.563	9.6	0.524
9YR	10.1	0.597	10.0	0.575
10-12YR	10.4	0.526	10.2	0.787

ULTRASOUND LIVER SPAN (MALE)



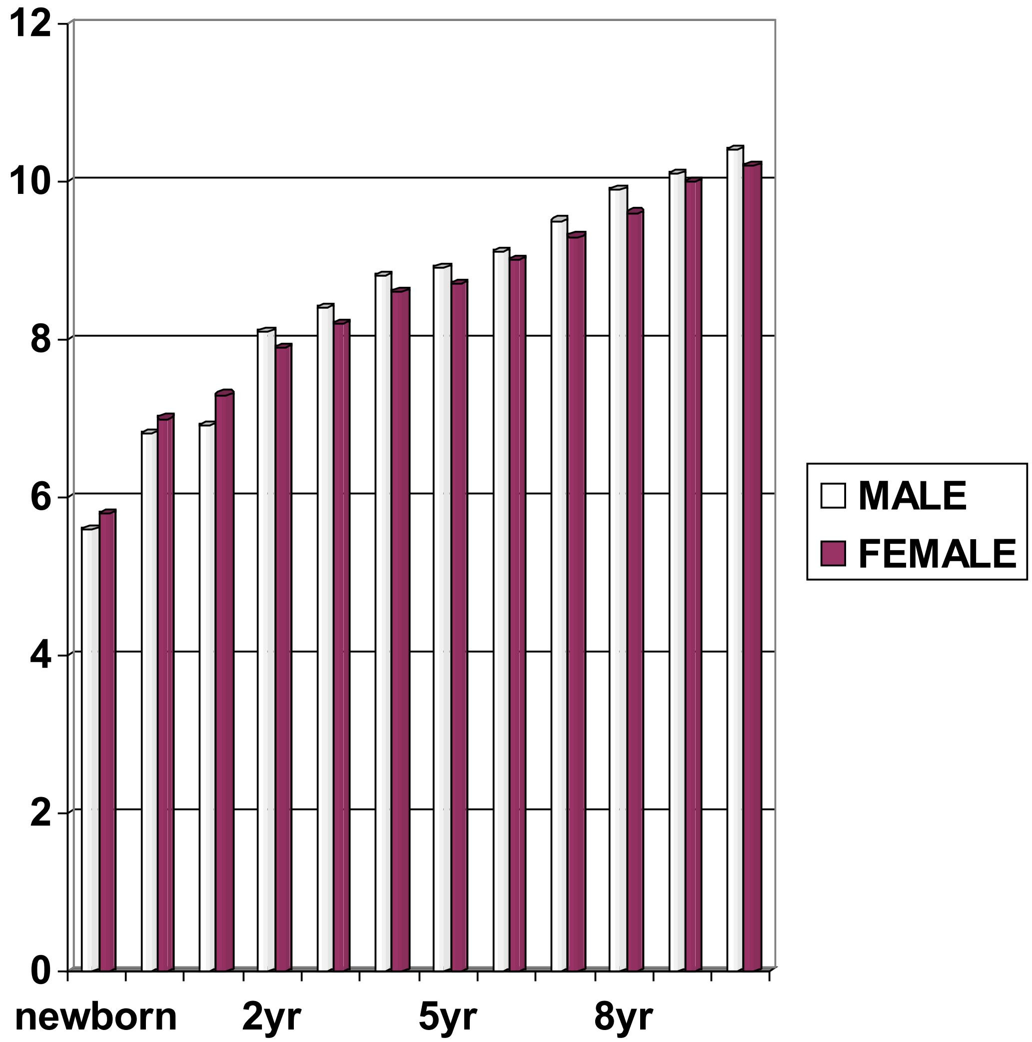
The mean liver span in boys by ultra sonogram ranges from 5.6 to 10.4cm from newborn period to 12years.

ULTRASOUND LIVER SPAN (FEMALE)



The mean liver span in girls by ultra sonogram ranges from 5.8 to 10.2cm from newborn period to 12years.

ULTRASOUND LIVER SPAN



The above bar diagram shows comparison of ultrasound liver span in male and female children. The liver span is found to be higher in boys after the age of 2years

ULTRASOUND LIVER SPAN

AGE	MALE	FEMALE	MEAN LIVER SPAN	STANDARD DEVIATION	95TH PERCENTILE
NEWBORN	5.6	5.8	5.7	0.375	6.2
INFANCY	6.4	6.6	6.5	0.742	8
1YR	6.9	7.3	7.1	0.703	8.6
2YR	8.1	7.9	8	0.717	9.2
3YR	8.4	8.2	8.3	0.564	9.3
4YR	8.8	8.6	8.7	0.370	9.4
5YR	8.9	8.7	8.8	0.545	9.9
6YR	9.1	9.0	9.05	0.558	10.3
7YR	9.5	9.3	9.4	0.680	10.5
8YR	9.9	9.6	9.75	0.560	10.7
9YR	10.1	10.0	10.05	0.583	11
10-12YR	10.4	10.2	10.3	0.670	11.4

Ultrasound liver span – male, female, mean liver span and 95th percentile are tabulated

In the newborn period, the mean liver span for boys is 5.6 cm. For girls of this age group is 5.8cm. In the newborn period, the mean liver span for girls is higher than the boys. Average liver span in newborn period is 5.7cm.

In infancy the mean liver span for boys is 6.4cm. For girls of this age group is 6.6cm. In infancy the mean liver span for girls is higher than the boys. Average liver span by ultrasound in infancy is 6.5cm.

In the one year age group, the mean liver span for boys is 6.9cm. For girls of this age group is 7.3cm. At one year the mean liver span for girls is higher than the boys. Average liver span by ultrasound in one year age group is 7.1cm.

In the two year age group, the mean liver span for boys is 8.1cm. For girls of this age group is 7.9cm. At two years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in two year age group is 8cm.

In the three year age group, the mean liver span for boys is 8.4cm. For girls of this age group is 8.2cm. At three years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in three year age group is 8.3cm.

In the four year age group, the mean liver span for boys is 8.8cm. For girls of this age group is 8.6cm. At four years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in four year age group is 8.7cm.

In the five year age group, the mean liver span for boys is 8.9cm. For girls of this age group is 8.7cm. At five years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in five year age group is 8.8cm.

In the six year age group, the mean liver span for boys is 9.1cm. For girls of this age group is 9cm. At six years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in six year age group is 9.05cm.

In the seven year age group, the mean liver span for boys is 9.5cm. For girls of this age group is 9.3cm. At seven years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in seven year age group is 9.4cm.

In the eight year age group, the mean liver span for boys is 9.9cm. For girls of this age group is 9.6cm. At eight years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in eight year age group is 9.75cm.

In the nine year age group, the mean liver span for boys is 10.1cm. For girls of this age group is 10cm. At nine years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in nine year age group is 10.05cm.

In the ten to twelve year age group, the mean liver span for boys is 10.4cm. For girls of this age group is 10.2cm. At ten to twelve years the mean liver span for boys is higher than the girls. Average liver span by ultrasound in ten to twelve year age group is 10.3cm.

INTER OBSERVER AGREEMENT BETWEEN CLINICAL I AND CLINICAL II

Intraclass correlation coefficient 0.87

95% Confidence Limit = 0.86, 0.88

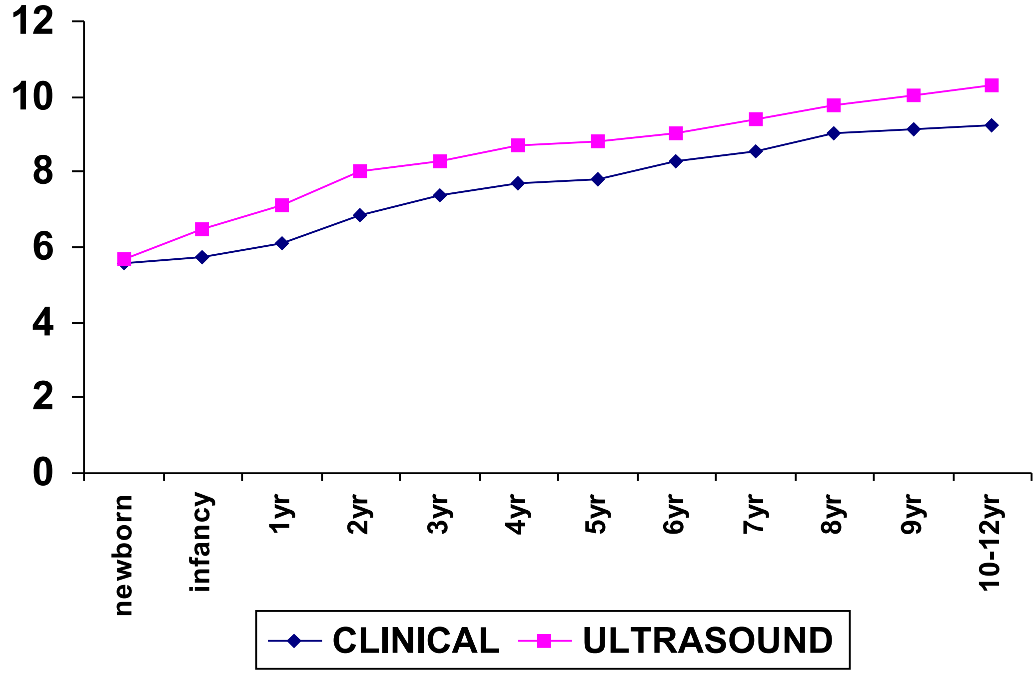
P value = 0.00

CLINICAL AND ULTRASOUND LIVER SPAN

AGE	CLINICAL	ULTRASOUND
Newborn	5.6	5.7
Infancy	5.75	6.5
1yr	6.1	7.1
2yr	6.85	8.0
3yr	7.4	8.3
4yr	7.7	8.7
5yr	7.8	8.8
6yr	8.3	9.05
7yr	8.55	9.4
8yr	9.05	9.75
9yr	9.15	10.05
10-12yr	9.225	10.3

Ultrasound liver span was higher than the clinical liver span in all age groups.

CLINICAL AND ULTRASOUND LIVER SPAN



CORRELATION BETWEEN CLINICAL AND ULTRASOUND LIVER SPAN

	Pearson's correlation r	p value
Overall	0.91	0.00
New born	0.84	0.00
Infancy	0.78	0.00
1yr	0.70	0.00
2yr	0.68	0.00
3yr	0.74	0.00
4yr	0.66	0.00
5yr	0.71	0.00
6yr	0.72	0.00
7yr	0.68	0.00
8yr	0.79	0.00
9yr	0.75	0.00
10-12yr	0.77	0.00

Clinical liver span correlates well with ultrasound liver span overall and in individual age groups.

CORRELATION OF LIVER SPAN WITH HEIGHT WEIGHT AGE AND SEX

	Pearson correlation r	**p valuve**
Height	0.89	0.00
Weight	0.86	0.00

r = correlation coefficient

	Spearman's correlation r	**p valuve**
Age	0.90	0.00

Ultrasound liver span has good correlation with age, height and weight.

Sex	**Liver span mean ± SD**	**p valuve**
Male	8.6 ± 1.5	0.44
Female	8.5 ± 1.3	

When ultrasound liver span was correlated with sex, there was no significant correlation.

UNIVARIATE LINEAR REGRESSION ANALYSIS

	Regression coefficient	95% confidence limits	p value
Age	**0.36**	**0.35, 0.38**	**0.00**
Height	**0.048**	**0.046, 0.05**	**0.00**
Weight	**0.18**	**0.17, 0.19**	**0.00**
Sex Male	**0.089**	**-0.14, 0.32**	**0.44**
Female	**0.0**		

Univariate regression analysis was done to analyse the influence of age, height and weight on ultrasound liver span. All the three are shown to influence liver size.

MULTIPLE LINEAR REGRESSION ANALYSIS

	Regression coefficient	95% confidence limits	p value
Age	**0.12**	**0.05, 0.19**	**0.00**
Height	**0.025**	**0.02, 0.03**	**0.00**
Weight	**0.031**	**0.01, 0.05**	**0.002**

Multiple linear regression analysis was done to find the independent influence of age, height and weight (corrected for other factors). All factors show an influence on the liver span. Age is the most important factor influencing liver span.

DISCUSSION

Liver size gives us information about the diagnosis and course of gastro intestinal and hematological diseases. Clinical liver span findings contribute to the clinical diagnosis and management, especially in emergency settings as in management of shock. Enlargement of liver can be the earliest sign of incipient cardiac failure. To determine whether a liver is enlarged significantly, it is important to establish the expected size. The clinical assessment of liver size by percussion is a simple practical measure of assessing liver size.

The accurate assessment of liver size is an important part of the clinical examination. Sheila Sherlock[5] states that “Percussion is a valuable method of determining liver size”, and in another context “an estimate of liver size… is important in monitoring progress”. Triger asserts that “Clinical examination of the liver should include percussion and size of the organ expressed as the liver span in centimeters in the mid-clavicular line”.

Clinical liver span measurement by percussion is prone for inter observer variation and there may be difference between clinical and ultrasound measurements. Further, palpation of liver in small children is different from the adults in that holding breath in inspiration needed for accurate palpation is rather difficult in children8. This study analyses the clinical measurement, ultrasound measurement, their correlation, significance of the difference and correlation with anthropometric parameters like age, sex, height and weight.

In the present study, the mean liver span clinically in the

Newborn age group – 5.6 cm

Infancy -5.8

1yr - 6.1

2yr - 6.8

3yr - 7.4

4yr -7.7

5yr - 7.8

6yr - 8.3

7yr - 8.6

8yr - 9.1

9yr - 9.2

10-12 yr - 9.3

Norms compiled by Naveh and Berant[28] for the liver span in various age groups after reviewing literature are as follows

Newborn -5.6-5.9cm

2 months -5cm

1 yr -6cm

2 yr – 6.5cm

3 yr -7 cm

4 yr – 7.5cm

5 yr – 8cm

6 yr onwards up to 12 yrs – 9 cm

There was 0.1cm to 0.7cm difference between the observations in various age groups between the present study and norms by Naveh and Berant.

Nelson[6] states liver span ranges from 4.5 to 5cm at one week of age to approximately 7-8cm in boys and 6-6.5 cm in girls by 12 years of age.

Measurable liver span by percussion ranged from 3.5cm to 10.5cm and increased curvilinearly with increasing age (p=0.00). In a similar study by Lawson et al[8], measurable liver span ranged from 1.5cm to 10.5cm, and increased curvilinearly with increasing age. In this respect the pattern of liver growth closely resembles that of body weight and height.

Statistical analysis of the results of measurements of the two observers (clinical1 and clinical2) was done by Intraclass correlation test and the intraclass correlation coefficient is 0.89 (p value =0.00). This indicates good agreement between the two observers. Clinical measurement of liver span shows good reliability. This is in concurrence with the study by Lawson et al[8], who studied the clinical liver span in infants and children, found no statistical difference between the measurements by the two examiners.

This is in contrast with the study by Joshi et al[9] regarding the accuracy and reliability of palpation and percussion for detecting hepatomegaly in which inter observer agreement between three physicians for the presence of hepatomegaly (using ultrasound as reference standard), at palpation (k=0.44-0.53) and percussion (k=0.17-0.33) showed poor reliability and accuracy. This study was done in the adult age group, with thicker chest walls and abdominal walls compared to children and hence may not be applicable to children

Diagnostic imaging techniques are superior to clinical examination in determining liver size[13,30]. The sonographic measurement of the liver size at mid-clavicular line was shown to be an easy and practical method for routine use in a study by Wolfgang Kratzer et al[15]. Sonography is routinely used to evaluate visceral organs in children because it offers numerous advantages[4]. There is no radiation, cost effective, portable, and non-invasive. It can be repeated if needed. Further the examination is real time, tri-dimensional and independent of organ function.

To date, however, there is a paucity of data regarding normal and borderline values and no uniform procedure for measuring the size of the liver has been established that can serve as a guideline for ultrasonographic examination of the liver. The method used in this study is oriented to the method described by Rumack et al[29].

Ultrasound has been found to be both accurate and reliable[2]. However despite wide spread clinical use, we know of no generally accepted standards of liver size in various age groups. In adults' sonographic measurements of normal liver span and correlation with sex, age, weight, height and body surface area was studied by Niedereau et al[2]. In the present study, the norms for various age groups by ultrasound measurement of liver span are established.

The correlation between clinical and ultrasound measurement shows there is good correlation between the clinical liver span measurements and ultrasound liver span measurements(r= 0.91). The correlation was tested age wise also, there is good between clinical and ultrasound liver span measurements.

In a study by Skrainka et al[10] they found that estimation of liver span by direct percussion was as accurate as ultrasound. But that by indirect percussion was inaccurate.

In a study by Chen CM et al[24] regarding clinical and ultrasound assessment in Chinese neonates the liver span measured by clinical methods with percussion and percussion/ palpation methods correlated well with that measured by ultrasound.

In the present study also when individual age groups were taken there was significant correlation between clinical and ultrasound liver span measurements in neonates.

The clinical liver span measurements were compared with the ultrasound measurements. There is a difference of up to 1.1cm in various age groups and ultrasound measurement is higher than clinical liver span measures.

CORRELATION WITH AGE

In the present study it is found, as the age increases, the liver span also increases. There is significant correlation between age and liver span by ultrasound (r = 0.90, p =0.00)

CORRELATION WITH SEX

In the newborns, infancy and one year, liver span of girls were more than that of boys. From two years of age, the liver span was comparatively more in boys throughout up to 12 years of age. This holds true for both clinical and ultrasound measurements. The well-known phenomenon that the male gastro intestinal organs are larger than the females has been already documented in studies using diagnostic imaging[31]. In autopsy studies also it is found that men have larger gastro intestinal organs than women[31].

In the present study, this sex difference is not statistically significant (p =0.44).

Similarly in a study regarding factors affecting liver size in adults by kratzer et al[15], their data showed, sex specificity was not clinically relevant. In a study by Lawson et a[18], liver growth in children appears to be sex specific. Age and sex were major influencing factors in their study.

In a similar study by Sarac et al[32] liver span in boys were more than the girls but was not statistically significant.

CORRELATION OF LIVER SPAN WITH HEIGHT AND WEIGHT

Correlation of liver span with height and weight were analyzed. Liver span has good independent correlation with both height and body weight(r = 0.89and0.86 respectively).

Castell et al[14] also have estimated the limits of normal liver span in adult Americans and correlated with height and weight. He found that liver span was best predicted using combination of height and weight. Height independent of sex was also an equally good predictor.

A correlate between organ size and weight in anthropometric findings is supported by ultrasound studies and studies based on autopsy finding[14].

In a similar study by safak et al[3] weight showed the strongest correlation to liver span.

In a similar study by konus et al[11] evaluated the normal liver size in 307 children by ultrasound and relationship of the dimensions with sex age, height and weight. Longitudinal diameter showed the best correlation with age, weight, and height. Height showed the strongest correlation of the all.

When Univariate regression analysis was done, age, height and weight exerted an influence on the liver span, whereas sex did not have significant influence.

In a study by kratzer et al[15] who studied the influence of multiple variables on liver size by means of co-variance analysis. Results of the multi-variate analysis showed that all the factors height, weight, sex and age exerted an influence on the liver span. Height was the most important factor influencing liver span.

When multiple linear regressions were done in our study, to find the independent influence of age, height and weight. All factors show an influence on the liver span. Age is the most important factor influencing liver span.

CONCLUSION

- Normal clinical and ultrasound liver span measurements in Indian pediatric population in various age groups are established.
- Inter observer agreement in clinical liver span measurement is good.
- Clinical liver span measurement correlates well with ultrasound liver span measurement. Hence, clinical liver span measurement by percussion is a reliable method.
- Age, weight and height are influencing factors on the liver span. Age is the most important factor influencing liver span.

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PROFORMA

s.no	na me	age	sex	Height (cm)	Weight (kg)	Clinical I cm	Clinical II cm	Ultrasound cm